

Knowledge Gaps & Potential New Directions

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Conflicts of Interest

Bracco Diagnostics: scientific advisory board, research support;
Guerbet: scientific advisory board, consultant, research support
Philips Healthcare: consultant, research support.

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- What are Gd retention rates/elimination rates with various GBCAs?
 - What conditions influence elimination rates?
 - What are baseline urine levels? Over time?
 - Measure other Lanthanides/metals as controls for environmental exposure?
- Postmortem tissue studies - human physiology; actual clinical conditions
 - What are average background levels of Gd in various organs?
 - Validate observations from preclinical & *in vivo* studies
 - Speciation
- Long term preclinical studies of various organs (Gd levels; histology; toxicity)
 - Extended PK >>24 hours
 - Mimic young subject receiving many GBCA doses.
 - Within each organ/tissue: where is Gd depositing? Diffuse or focal? Intracellular/Extracellular?
- Define vulnerable populations? Infants/children; conditions receiving multiple exposures; elderly?
 - What are risks to development? To degenerative diseases in later life?
 - Are there special populations at increased risk in various organs: e.g. iron overload (liver, spleen, bone marrow); lead poisoning/heavy metal poisoning; bone mineralization disorders
 - Potential medication interactions resulting in supra-physiologic amounts of cations competing for transmetallation.

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Additional gaps - lessor priority

- Need sensitive, reproducible, non-invasive method for measuring Gd *in vivo*
 - Techniques: Xray fluorescence; Neutron activation analysis; other?
- Is chelation therapy needed? Best method?
 - Deferoxamine shown to reduce Gd liver levels - what is mechanism?
- Encourage collaborations across disciplines and areas of expertise
 - Identify centers of excellence for Gd measurement; speciation; EM
 - Centers with access to postmortem tissue collection